A PROSPECTIVE, MULTI-CENTER, RANDOMIZED, MASKED, CONTROLLED, POST-MARKET STUDY OF USE OF THE OMNI® SURGICAL SYSTEM IN COMBINATION WITH CATARACT EXTRACTION IN OPEN ANGLE GLAUCOMA [redacted]

PROTOCOL ID #: [redacted]

CURRENT REVISION: Rev A

REVISION DATE: July 31, 2020

SPONSOR:
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Agreement of Principal Investigator

I, _____ agree to conduct this trial in accordance with this clinical protocol and any amendments.

_____ _____
Signature Date

_____ _____
Center Name City, State, Country

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Revision History

Revision	Date Issued	ECO
[redacted]	[redacted]	[redacted]

TABLE OF CONTENTS

1 PROTOCOL SYNOPSIS 5

2 STUDY OBJECTIVE 8

3 BACKGROUND AND JUSTIFICATION FOR THE STUDY 8

4 STUDY DEVICE 11

4.1 Indications For Use 11
4.2 Device Description 11
4.3 Training 13

5 STUDY DESIGN 13

5.1 Study Device 13
5.2 Study Sites 13

6 STUDY ENDPOINTS 13

6.1 Effectiveness Endpoints 13
6.2 Safety Endpoints 14

7 STUDY SELECTION CRITERIA 14

7.1 Inclusion Criteria 14
7.2 Exclusion Criteria 15

8 STUDY PROCEDURES 16

8.1 Study Schedule 16
8.2 Number of Subjects, Duration of Follow-up and Study Duration 17
8.3 Informed Consent and Point of Enrollment 17
8.4 Screening Visit 18
8.5 Washout of Hypotensive Medications 18
8.6 Baseline Visit 19
8.7 Surgical Procedure 20
8.8 Follow-Up Visits 20
8.9 Unscheduled Visits 21
8.10 Management of IOP After Surgery 21
8.11 Withdrawal and Discontinuation 22
8.12 Subjects Lost to Follow-up 23

9 ADVERSE EVENTS (AES) 23

9.1 Definitions of AE, SAE, SADE, USADE 23
9.2 List of Anticipated Potential Adverse Events 24
9.3 Reporting Adverse Events and Unanticipated Adverse Device Effects 25

10 STATISTICAL CONSIDERATIONS 26

10.1 Sample Size Calculation 26
10.2 Analysis Populations 26
10.2.1 Safety Population 27
10.2.2 As Treated 27
10.3 Demographics and Baseline Characteristics 28
10.4 Effectiveness Endpoints and Analysis Methods 28
10.4.1 Primary Effectiveness Endpoint 28

10.4.2 Sensitivity Analysis 29
10.4.3 Covariate Analysis 30
10.4.4 Other Important Clinical Effectiveness Outcomes 30
10.4.5 Additional Effectiveness Analyses 31
10.5 Safety Analysis 32
10.5.1 Adverse Event 32
10.5.2 Best Corrected Visual Acuity (BCVA) 32
10.5.3 Other Safety Outcomes 32
10.6 Interim Analysis 33
10.7 Deviation from the Statistical Plan 33
11 MONITORING PROCEDURES 33
12 DATA AND QUALITY MANAGEMENT 34
12.1 Database Management 34
12.2 Subject Identification 34
12.3 Subject Accountability 35
12.4 Confidentiality 35
12.5 Source Data and Case Report Forms 35
12.6 Retention Period 35
13 PROTOCOL MODIFICATIONS AND DEVIATIONS 36
14 DEVICE FAILURES AND MALFUNCTIONS 36
15 ETHICAL CONSIDERATIONS 36
15.1 Declaration of Helsinki 36
15.2 Institutional Review Boards (IRB) 36
15.3 Informed Consent Document (ICD) 37
15.4 Public Listing of Study 37
16 STUDY ADMINISTRATION 37
16.1 Early Termination or Suspension of the Study or an Investigational site 37
16.2 Investigator Responsibilities 38
16.2.1 General Responsibilities of Investigators 38
16.2.2 Specific Responsibilities of Investigators 38
16.2.3 Investigator Records 38
16.2.4 Investigator Reports 39
16.3 Investigator Agreement 39
17 PUBLICATION POLICY 40
18 BIBLIOGRAPHY 41
19 APPENDIX A – METHODS FOR EXAMS, TESTS AND QUESTIONNAIRES 43
19.1 List of Study procedures 43
19.2 PRO 44
19.3 Visual Acuity with manifest refraction 44
19.4 Measurement of intraocular pressure 45
19.5 Visual Field Examination 49
19.6 Dilated fundus examination 49
19.7 Slit Lamp Examination 49
19.8 Gonioscopy 52
19.9 Ocular Hypotensive Medications 52
20 APPENDIX B - DECLARATION OF HELSINKI 53

1 PROTOCOL SYNOPSIS

Protocol Title	A Prospective, Multi-center, Randomized, Controlled, Masked, Post-market Study of use of the OMNI® Surgical System in Combination with Cataract Extraction in Open Angle Glaucoma [redacted]
Protocol ID Number	[redacted]
Study Device	OMNI® Surgical System
Control Group or Device	[redacted]
Study Objective	First, to prospectively compare the clinical effect of the transluminal viscoelastic delivery and trabeculotomy using the OMNI Surgical System to the [redacted] used with Cataract Extraction in eyes with open angle glaucoma (OAG) and second, to prospectively compare the clinical effect of the transluminal viscoelastic delivery using the OMNI Surgical System to the [redacted] used with Cataract Extraction in eyes with open angle glaucoma (OAG)
Study Design	Randomized, controlled, multi-center, post-market prospective study
Primary Effectiveness Endpoint	Primary inference will be based on a planned analysis when all subjects have completed the 12-month visit. • Mean change in unmedicated DIOP from baseline at the 12-month postoperative examination
Other Effectiveness Endpoints	• Proportion of eyes with a ≥ 20% decrease in **unmedicated** mean diurnal IOP (DIOP) from baseline • Proportion of eyes with **unmedicated** mean DIOP between 6 and 18 mmHg inclusive • Mean change in the number of ocular hypotensive medications compared to Screening • Percent change in **unmedicated** DIOP from baseline
Safety Endpoints	• Rates of ocular adverse events (intraoperative, postoperative) • Reduction in best corrected distance visual acuity (BCVA) from baseline (note: reduction in BCVA due to posterior capsular opacity (PCO) will not be treated as a safety event) • Secondary Ocular Surgical Interventions, including laser, for IOP control

Inclusion Criteria	At least one eye of each participating subject should meet inclusion criteria. 1. Male or female subjects, 22 years or older. 2. Visually significant cataract. 3. Diagnosed with mild to moderate open angle glaucoma (e.g. primary open angle glaucoma, pigmentary glaucoma, pseudoexfoliative glaucoma) as documented in subjects' medical record substantiated using funduscopic exam or OCT and at least one visual field test using the SITA Standard 24-2 testing algorithm. o [redacted] o [redacted] 4. [redacted] 5. At baseline, unmedicated diurnal IOP 24-39 mmHg and IOP at least 3 mmHg higher than screening IOP. 6. Scheduled for cataract extraction followed by either: a) ab-interno transluminal viscoelastic delivery with trabeculotomy using OMNI surgical System b) ab-interno transluminal viscoelastic delivery using OMNI surgical System c) [redacted]. 7. Shaffer grade of ≥ III in all four quadrants. 8. Potential of good best corrected visual acuity post cataract extraction, in the investigator's judgment 9. Able and willing to comply with the protocol, including all follow-up visits. 10. Understand and sign the informed consent.

Exclusion Criteria	A subject who meets any of the exclusion criteria listed below will not receive the study procedure: 1. Any of the following prior treatments for glaucoma: o Laser trabeculoplasty ≤3 months prior to baseline o Implanted with iStent (All types), Cypass, Xen, Express, glaucoma draining device/valve, or Hydrus Device o Prior canaloplasty, goniotomy, trabeculotomy, trabeculectomy, ECP or CPC 2. Acute angle closure, normal tension, traumatic, congenital, malignant, uveitic, neovascular or severe glaucoma as documented in subjects' medical record. 3. Concurrent IOP-lowering procedure other than one of the study procedures listed under inclusion criterion 6 at the time of cataract surgery (e.g. ECP, CPC, etc.) 4. In the Investigator's judgement, predisposed to significant risk because of washout of ocular hypotensive medications. 5. Concurrent ocular pathology or systemic medical condition which, in the Investigator's judgment, would either place the subject at increased risk of complications, contraindicate surgery, place the subject at risk of significant vision loss during the study period (e.g., wet AMD, corneal edema, Fuch's dystrophy, active intraocular infection or inflammation within 30 days prior to Screening Visit, etc.), or interfere with compliance to elements of the study protocol (e.g., returning to Investigator's office for follow-up visits). 6. History of penetrating keratoplasty or another corneal transplant; corneal abnormality that would prevent reliable IOP measurement; e.g. kearatoconus or abnormally thick or thin cornea. 7. BCVA of logMAR 1.0 (20/200) or worse in the fellow eye not due to cataract. 8. Participation (≤ 30 days prior to baseline) in an interventional trial which could have a potential effect on the study outcome, as determined by the study investigator. 9. Women of childbearing potential if they are currently pregnant or intend to become pregnant during the study period; are breast-feeding; or are not in agreement to use adequate birth control methods to prevent pregnancy throughout the study.

Number of Subjects Enrolled and Treated	Approximately 459 [redacted] to complete 411 [redacted] at 12 months postoperative assuming approximately 10% drop-out rate
Study Duration for each Subject	Up to 40 months
Number of Sites	Up to 30 study sites in US
Schedule of Visits	Screening, Baseline, Surgery (Day 0), Day 1, Week 1, Month 1, 3, 6, 12, 18, 24, 36 Additional post-washout visits will be scheduled for the subjects who are on medications at 12, 24 and 36 months.
Randomization	1:1:1
Treatments	•Ab-interno transluminal viscoelastic delivery (up to 360 degrees) and trabeculotomy (at least 180 degrees and up to 360 degrees) using the OMNI Surgical System •Ab-interno transluminal viscoelastic delivery (up to 360 degrees) using the OMNI Surgical System • [redacted]

2 STUDY OBJECTIVE

First, to prospectively compare the clinical effect of the transluminal viscoelastic delivery and trabeculotomy using the OMNI Surgical System [redacted] used with Cataract Extraction in eyes with open angle glaucoma (OAG) and second, to prospectively compare the clinical effect of the transluminal viscoelastic delivery using the OMNI Surgical System [redacted] used with Cataract Extraction in eyes with open angle glaucoma (OAG).

3 BACKGROUND AND JUSTIFICATION FOR THE STUDY

Glaucoma is a progressive disease leading to irreversible damage to retinal ganglion cells with the global burden expected to rise to 111.8 million people by the year 2040.[1] OAG is the most prevalent form of glaucoma and it's proven that lowering IOP is the only efficient way to slow down the progressive optic nerve damage and visual field loss.[2] Hypotensive eye drops are commonly used as the first line clinical management for

[1] Tham YC, Li X, Wong TY, et al. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. Ophthalmology. 2014;121:2081–2090.
[2] European Glaucoma Society. Terminology and guidelines for glaucoma 4th edition Savona, Italy: Editrice PubliComm, 2014.

OAG.[3] Ocular side effects such as allergies, ocular surface disorders, blepharitis, pemphigoid, abnormal pigmentation etc. and systemic side effects such as bradycardia, headaches, depression, anxiety, confusion, dysarthria, hallucinations, lethargy, polyuria, weight loss, metabolic acidosis, etc. can occur during long term use of topical medications for management of OAG. [4] There is also a documented low rate of compliance and tolerability with eye drops that results in disease progression and loss of vision.[5] The cost of these chronic medications and difficulty administering drops to the eyes contributes to poor compliance.

The Ocular Hypertension Treatment Study showed that reduction of IOP by an average of 22.5% through medical intervention decreased conversion from ocular hypertension to glaucoma over a 5-year period to approximately half that of untreated controls (4.4 vs. 9.5%).[4] Similarly, the EMGT showed that treatment of newly diagnosed primary OAG with argon laser trabeculoplasty plus betaxolol reduced the risk of disease progression at 6 years to half of that for untreated controls (hazard ratio, 0.50; 95% confidence interval, 0.35–0.71).[6] Each mmHg of IOP reduction decreased the risk of progression by approximately 10%.[7] AGIS showed that eyes with 100% of visits with IOP less than 18 mmHg over 6 years had mean changes from baseline in visual field defect score close to zero during follow-up.[7]

Minimally (or micro) invasive glaucoma surgery (MIGS) provides an alternative to more invasive surgical methods (i.e. trabeculectomy or glaucoma drainage devices) or to laser procedures. MIGS procedures can generally be done along with cataract surgery minimizing additional risk or as standalone procedures. Several studies have demonstrated MIGS to provide long-term IOP lowering and the potential to reduce or eliminate the need for medications (and therefore reliance on patient adherence).[8,9]

MIGS techniques that re-establish the aqueous outflow through the physiological pathways are gaining acceptance among glaucoma surgeons. Canaloplasty (originally

[3] Kass MA, Heuer DK, Higginbotham EJ, Johnson CA, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol. 2002; 120:701–713.

[4] Kenji Inoue. Managing adverse effects of glaucoma medications. Clin Ophthalmol. 2014; 8: 903–913. Published online 2014 May 12. doi: 10.2147/OPTH.S44708.

[5] Newman-Casey PA, Robin AL, Blachley T, Farris K, Heisler M, Resnicow K, Lee PP. The Most Common Barriers to Glaucoma Medication Adherence: A Cross-Sectional Survey. Ophthalmology. 2015 Jul; 122(7):1308-16.

[6] Leske MC, Heijl A, Hussein M, et al. Factors for glaucoma progression and the effect of treatment: The Early Manifest Glaucoma Trial. Arch Ophthalmol 2003;121:48–56.

[7] The Advanced Glaucoma Intervention Study (AGIS): the relationship between control of intraocular pressure and visual field deterioration. The AGIS Investigators. Am J Ophthalmol 2000;130:429–40.

[8] Francis BA, Singh K, Lin SC, et al. Novel glaucoma procedures: a report by the American Academy of Ophthalmology. Ophthalmology 2011;118:1466–1480.

[9] Vinod K, Gedde SJ. Clinical investigation of new glaucoma procedures. Curr Opin Ophthalmol 2017;28:187–193.

described as ab externo) is one such procedure that is intended to restore the natural aqueous outflow system through microcatheterization and viscodilation of Schlemm's canal with a well-documented safety and efficacy profile in reducing IOP.[10,11,12] Trabeculotomy is another such procedure that relieves the resistance to aqueous flow by cleaving the trabecular meshwork and the inner wall of Schlemm's canal, resulting in pressure reductions.[13,14]

The OMNI™ Surgical System (Sight Sciences Inc, Menlo Park, CA) is a 510K-cleared manually operated device indicated for the delivery of small amounts of viscoelastic fluid and to cut trabecular meshwork tissue during trabeculotomy procedures. The OMNI™ Surgical System allows doctors to perform viscodilation of Schlemm's canal in conjunction with trabeculotomy through single clear corneal incision. [15,16,17]

Cataract is often seen as a comorbidity present in patients with glaucoma and together they serve as leading causes of blindness worldwide.[18] Cataract accounts for 33% of visual disability worldwide and may have a causal relationship with increased IOP in

[10] Francis BA, Singh K, Lin SC, et al. Novel glaucoma procedures: a report by the American Academy of Ophthalmology. Ophthalmology 2011;118:1466–1480.
[11] Vinod K, Gedde SJ. Clinical investigation of new glaucoma procedures. Curr Opin Ophthalmol 2017;28:187–193.
[12] Lewis RA, von Wolff K, Tetz M, et al. Canaloplasty: circumferential viscodilation and tensioning of Schlemm canal using a flexible microcatheter for the treatment of open-angle glaucoma in adults. Two-year interim clinical study results. J Cataract Refract Surg 2009;35:814-824.
[13] Sarkisian SR, Mathews B, Ding K, et al. 360°ab-interno trabeculotomy in refractory primary open-angle glaucoma. Clin Ophthalmol 2019;13:161-168.
[14] Grover DS, Smith O, Fellman RL, et al. Gonioscopy-assisted transluminal trabeculotomy: an ab interno circumferential trabeculotomy: 24 months follow-up. J Glaucoma 2018;27:393-401.
[15] Clara Martinez-Rubio, Ioan Alexandru Placinta, Rodrigo Molina-Pallete, Paula Martínez Lopez-Corell, Jorge Vila-Arteaga. OMNI-an initial experience with a new surgical glaucoma treatment device. ESCRS 2018.
[16] Iwona Grabska-Liberek, Julita Majszyk-Ionescu, Agnieszka Skowyra, Monika Rogowska, Anna Plichta, Patrycja Duda, Ingrid Kane OMNI 360TM in Open-Angle Glaucoma Treatment: A 6-month Follow-up. ESCRS 2018.
[17] Paula Martínez Lopez-Corell, Rodrigo Molina-Pallete, Clara Martinez-Rubio, Ioan Alexandru Placinta, Jorge Vila-Arteaga Procedural Steps For OMNI, A New Surgical Technique For Glaucoma Treatment, In Combination With Cataract Surgery ESCRS 2018.
[18] Resnikoff S, Pascolini D, Etya'ale D, Kocur I, Pararajasegaram R, Pokharel GP, Mariotti SP Bull World Health Organ. Global data on visual impairment. 2016 Nov; 82(11):844-51.

OAG.[19] Cataract surgery is known to reduce IOP in glaucoma patients. Combined glaucoma and cataract surgery often result in a greater decrease in IOP and use of glaucoma medications compared with cataract surgery alone.[20,21] When a patient with glaucoma also requires surgical intervention for cataract, the ophthalmologist often performs simultaneous cataract and glaucoma surgery.

Note: A summary of known and potential risks to humans, as identified in the literature or through preclinical testing and/or prior clinical evaluations for the study devices can be found in the Instructions for Use for the OMNI Surgical System [redacted]

This prospective, multicenter, randomized controlled, post-market clinical trial will evaluate and compare clinical outcomes of i) ab-interno transluminal viscoelastic delivery and trabeculotomy using OMNI™ Surgical System, ii) ab-interno transluminal viscoelastic delivery using the OMNI™ Surgical System and iii) TM implantation [redacted] in patients with mild to moderate open angle glaucoma undergoing cataract surgery.

4 STUDY DEVICE

4.1 INDICATIONS FOR USE

The OMNI Surgical System has been 510k cleared by the US Food and Drug Administration (FDA) for the following indication for use:

> The OMNI® PLUS Surgical System is a manually operated device for delivery of small amounts of viscoelastic fluid, for example Healon® PRO or Healon GV® PRO from Johnson & Johnson Vision, Amvisc® from Bausch & Lomb, or PROVISC® from Alcon, during ophthalmic surgery. It is also indicated to cut trabecular meshwork tissue during trabeculotomy procedures.

4.2 DEVICE DESCRIPTION

The OMNI™ Surgical System ("OMNI") is a sterile, single use, manually operated instrument used by ophthalmologists to deliver small, controlled amounts of viscoelastic

[19] Bourne RRA, Stevens GA, White RA, et al. Causes of vision loss worldwide, 1990-2010: a systematic analysis. Lancet Glob Heal. 2013;1:339–349.

[20] Zhang ML, Hirunyachote P, and Jampel H. Combined surgery versus cataract surgery alone for eyes with cataract and glaucoma. Cochrane Database Syst Rev. 2015; 7: CD008671

[21] Vold S, Ahmed II, Craven ER, Mattox C, Stamper R, Packer M, Brown RH, Ianchulev T; CyPass Study Group. Two-Year COMPASS Trial Results: Supraciliary Microstenting with Phacoemulsification in Patients with Open-Angle Glaucoma and Cataracts. Ophthalmology. 2016 Oct;123(10):2103-12. doi: 10.1016/j.ophtha.2016.06.032.

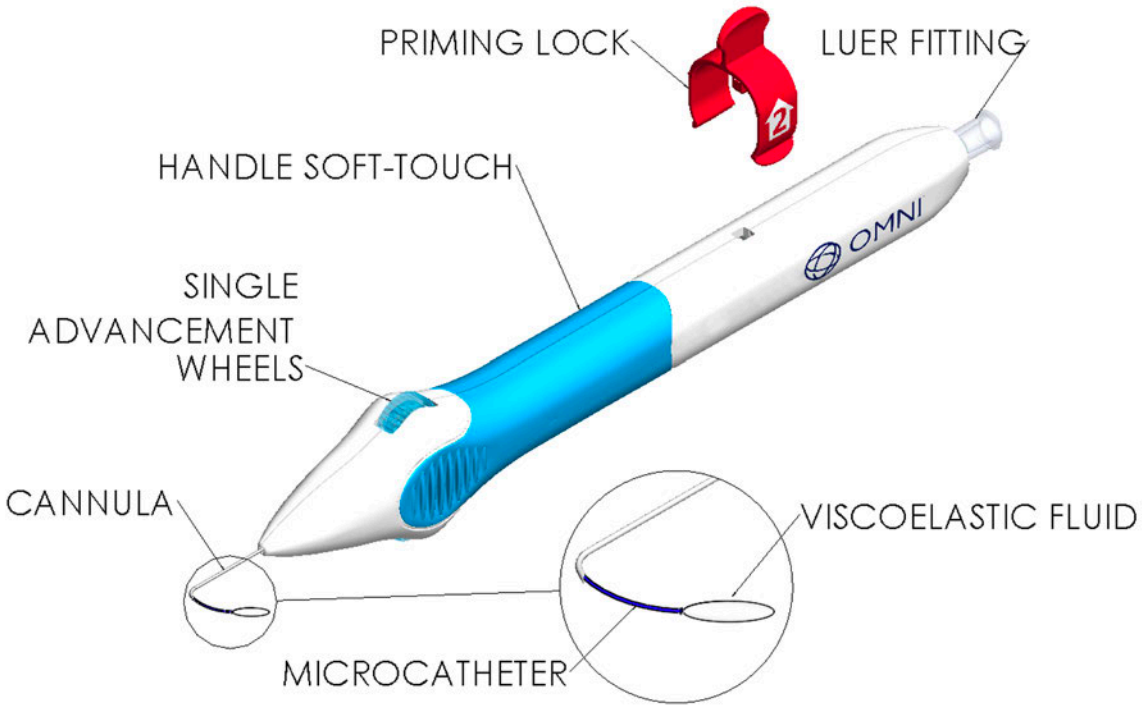
into the anterior segment of the eye during ophthalmic surgery. It is also indicated to cut trabecular meshwork tissue during trabeculotomy procedures.

The OMNI is designed to function with commonly used viscoelastic fluids made commercially available by companies such as Abbott Medical Optics (AMO), Bausch & Lomb, and Alcon. The OMNI dispenses fluid on the principle of exchanging volumes much like a syringe. The handheld instrument includes a cannula, microcatheter, internal reservoir and plunger tube, and finger wheels. The finger wheels on the handle of the device are used to advance and retract the microcatheter. In addition, when the device is being used to deliver viscoelastic, retraction of the microcatheter causes the plunger tube to advance into the viscoelastic fluid reservoir thereby dispensing viscoelastic fluid.

The microcatheter can be advanced/retracted up to 20 mm per cycle. The microcatheter can be fully advanced/retracted up to 5 times (i.e. 5 full cycles of 20 mm each). Dispensation of viscoelastic can only occur during the first two 20-mm cycles.

The OMNI can deliver approximately 5.5 microliters of viscoelastic in each 20 mm cycle (total volume = 11 microliters). The Plus configuration can deliver approximately 10.5 microliters of viscoelastic in each 20 mm cycle. The total volume of viscoelastic that can be delivered by the OMNI Plus is approximately 21 microliters.

Figure 1: OMNI Surgical System



4.3 TRAINING

Investigators participating in the study must be experienced in using the OMNI 2.0 (OMNI NextGen) Surgical System. All study staff will receive training on the protocol and execution of the study according to applicable regulations and Good Clinical Practices.

5 STUDY DESIGN

This is a prospective, randomized, controlled, multicenter, comparative study in which a total of 459 subjects will be randomized in an equal allocation ratio (1:1:1) to either the OMNI (transluminal viscoelastic delivery AND trabeculotomy), OMNI (transluminal viscoelastic delivery only), or [redacted] and followed for 36 months after surgery.

The study will employ a medication washout [redacted] which eliminates the potential confounding influence of ocular hypotensive medications in the assessment of device effectiveness.

5.1 STUDY DEVICES

The study device is the OMNI Surgical System. Subjects randomized to one of the two OMNI treatment groups will undergo either

•Ab-interno transluminal viscoelastic delivery (up to 360 degrees) and trabeculotomy (at least 180 degrees and up to 360 degrees) using the OMNI Surgical System

•Ab-interno transluminal viscoelastic delivery (up to 360 degrees) using the OMNI Surgical System

The Comparator group is the [redacted].

5.2 STUDY SITES

This study will be conducted at up to 30 sites in the United States.

6 STUDY ENDPOINTS

6.1 EFFECTIVENESS ENDPOINTS

The **Primary effectiveness endpoint** is:

- Mean change in unmedicated DIOP from baseline at 12-month postoperative examination

Other effectiveness endpoints are:

- Proportion of eyes with a ≥ 20% decrease in **unmedicated** mean diurnal IOP (DIOP) from baseline
- Proportion of eyes with **unmedicated** mean DIOP between 6 and 18 mmHg inclusive
- Mean change in the number of ocular hypotensive medications compared to Screening
- Percent change in **unmedicated** DIOP from baseline

6.2 SAFETY ENDPOINTS

Safety will be assessed by evaluating the following measures over time:

- Rates of ocular adverse events (intraoperative, postoperative)
- Reduction in best corrected distance visual acuity (BCVA) from baseline (note: reduction in BCVA due to posterior capsular opacity (PCO) will not be treated as a safety event)
- Secondary Ocular Surgical Interventions, including laser, for IOP control

7 STUDY SELECTION CRITERIA

7.1 INCLUSION CRITERIA

At least one eye of each participating subject should meet inclusion criteria.

1. Male or female subjects, 22 years or older.
2. Visually significant cataract.
3. Diagnosed with mild to moderate open angle glaucoma (e.g. primary open angle glaucoma, pigmentary glaucoma, pseudoexfoliative glaucoma) as documented in subjects' medical record substantiated using funduscopic exam or OCT and at least one visual field test using the SITA Standard 24-2 testing algorithm.
   - [redacted]
4. At screening, [redacted] on 1-5 IOP-lowering medications(For combination IOP-lowering medications that consist of two or more IOP-lowering drugs, each IOP-lowering drug component counts as a separate medication.) with a stable medication regimen for at least two months prior to screening visit.

5. At baseline, [redacted] IOP at least 3 mmHg higher than screening IOP.
6. Scheduled for cataract extraction followed by either:
   a) ab-interno transluminal viscoelastic delivery with trabeculotomy using OMNI surgical System
   d) ab-interno transluminal viscoelastic delivery using OMNI surgical System
   e) [redacted]
7. Shaffer grade of ≥ III in all four quadrants.
8. Potential of good best corrected visual acuity post cataract extraction, in the investigator's judgment
9. Able and willing to comply with the protocol, including all follow-up visits.
10. Understand and sign the informed consent.

7.2 EXCLUSION CRITERIA

A subject who meets any of the exclusion criteria listed below will not receive the study procedure:

1. Any of the following prior treatments for glaucoma:
   - Laser trabeculoplasty ≤3 months prior to baseline
   - Implanted with iStent (All types), Cypass, Xen, Express, glaucoma draining device/valve, or Hydrus Device
   - Prior canaloplasty, goniotomy, trabeculotomy, trabeculectomy, ECP or CPC
2. Acute angle closure, normal tension, traumatic, congenital, malignant, uveitic, neovascular or severe glaucoma as documented in subjects' medical record.
3. Concurrent IOP-lowering procedure other than one of the study procedures listed under inclusion criterion 6 at the time of cataract surgery (e.g. ECP, CPC, etc.)
4. In the Investigator's judgement, predisposed to significant risk because of washout of ocular hypotensive medications.
5. Concurrent ocular pathology or systemic medical condition which, in the Investigator's judgment, would either place the subject at increased risk of complications, contraindicate surgery, place the subject at risk of significant vision loss during the study period (e.g., wet AMD, corneal edema, Fuch's dystrophy, active intraocular infection or inflammation within 30 days prior to Screening Visit, etc.), or interfere with compliance to elements of the study protocol (e.g., returning to Investigator's office for follow-up visits).
6. History of penetrating keratoplasty or another corneal transplant; corneal abnormality that would prevent reliable IOP measurement; e.g. kearatoconus or abnormally thick or thin cornea.
7. BCVA of logMAR 1.0 (20/200) or worse in the fellow eye not due to cataract.
8. Participation (≤ 30 days prior to baseline) in an interventional trial which could have a potential effect on the study outcome, as determined by the study investigator.
9. Women of childbearing potential if they are currently pregnant or intend to become pregnant during the study period; are breast-feeding; or are not in agreement to use adequate birth control methods to prevent pregnancy throughout the study.

8 STUDY PROCEDURES

8.1 STUDY SCHEDULE

8.2 NUMBER OF SUBJECTS, DURATION OF FOLLOW-UP AND STUDY DURATION

Approximately 459 subjects will be randomized (1:1:1) to treatment, [redacted] No site will randomize more than 25% of the total number of subjects without prior approval from Sponsor.

[redacted]

Study subject participation will be from approximately 35 months, (at a minimum) to 40 months, depending on the length of the required medication washout prior to baseline and if additional washout is needed [redacted] for subjects presenting at these visits with ocular hypotensive medication.

It is anticipated that the enrollment period for the study will last approximately 24 months. Including the 40-month follow-up period, the study is expected to last 54 months.

8.3 INFORMED CONSENT AND POINT OF ENROLLMENT

The IRB-approved informed consent will be presented and explained to each prospective subject by the investigator or a trained clinical professional. Once the subject has had ample time to read the consent form, has been informed of all aspects of the study, and has had an opportunity to ask questions, the subject will be given a choice to voluntarily confirm his or her participation in the study as documented by completion of the Informed Consent. After signing the Informed Consent and the HIPAA (Health Insurance Portability and Accountability Act) authorization, the subject can then proceed with the screening visit. The subject has the right to withdraw from the study at any time without consequences, as indicated in the Informed Consent Document.

The subject's signed and dated informed consent must be obtained before conducting any study specific procedures that are not part of the standard of care. Subjects are enrolled upon signing the ICD even if they subsequently fail to meet the eligibility criteria.

The principal investigator(s) must retain the original, signed written Informed Consent Document. A copy of the written Informed Consent Document must be given to the subject.

8.4 SCREENING VISIT

After obtaining an understanding of the purpose of this study, then reviewing and signing the Informed Consent Document, all potential subjects will undergo an initial screening examination in order to determine their eligibility for the study. Exams and tests listed in the Screening column of Table 1 should be performed. Refer to Appendix A for instructions for performing the exams.

[redacted]

Exam data collected on subjects prior to enrollment as part of the routine clinical practice may serve as Screening data as long as it was collected within 15 days prior to the visit. The only exceptions to this are:

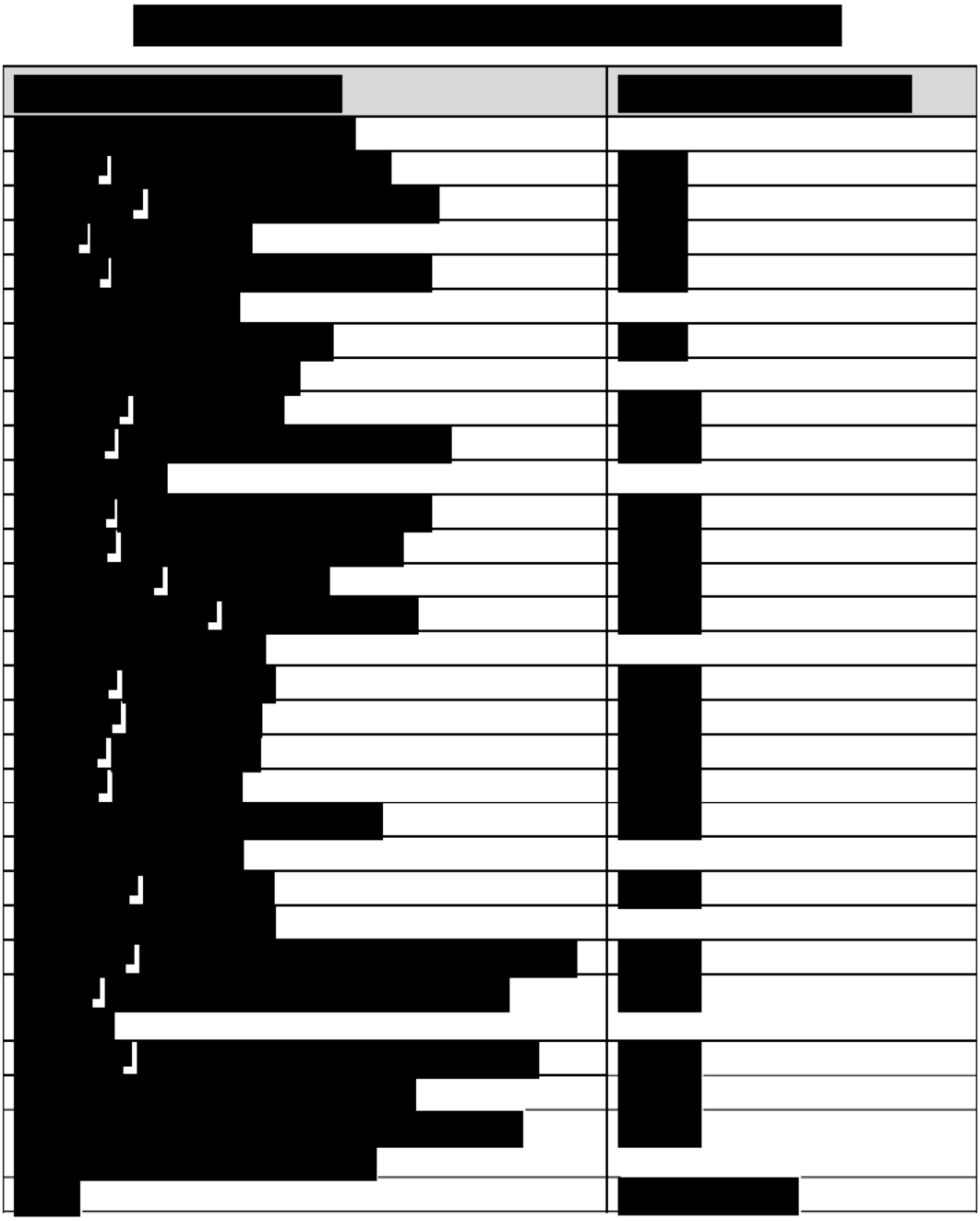
- IOP and IOP-lowering medications. These data must be collected at the Screening visit.
- Visual field: Visual Fields conducted per the protocol method (Humphrey 24-2 SITA standard) within 6 months of the screening visit will be acceptable.

8.5 WASHOUT OF HYPOTENSIVE MEDICATIONS

Subjects on ocular hypotensive medication who meet all eligibility criteria at the screening visit will be instructed to discontinue their ocular hypotensive medication regimen, and to return for a Baseline visit after completing the appropriate washout period. The final eligibility assessment will happen at baseline visit.

[redacted]

If the study subject fails to remember to not use ocular hypotensive medication for the study eye per the required washout period, they can be reinstructed to restart washout and return for the Baseline or other washout IOP visits as long as it falls within the specified visit window. If deemed necessary by the PI, a subject can be given hypotensive medications after the baseline visit until the day of surgery. An oral hypotensive medication can be used between baseline to surgery. The minimum wash-out periods are specified in Table 2 below.



8.6 BASELINE VISIT

After appropriate washout during the Baseline visit, the exams and tests listed in the Baseline column of Table 1 should be performed in order to determine final eligibility for the study. If both eyes meet the applicable inclusion and exclusion criteria, the eye with higher IOP will be included in the study. In case of both eyes with same IOP at baseline,

investigator will select the study eye. Subjects meeting all criteria at the Baseline Visit will be scheduled for surgery and be randomized to a treatment arm. Randomization to treatment group will be performed using a 1:1:1 ratio and will be stratified by site. Computer-generated randomization will be administered through the electronic data capture (EDC) system with separate randomization sequences for each clinical site.

Refer to Appendix A for instructions for performing the exams.

8.7 SURGICAL PROCEDURE

Only eyes with uneventful cataract extraction will receive one of the following surgical procedures based on randomization:

1. Ab-interno transluminal viscoelastic delivery (up to 360 degrees) and trabeculotomy (at least 180 degrees and up to 360 degrees) using the OMNI Surgical System
2. Ab-interno transluminal viscoelastic delivery (up to 360 degrees) using the OMNI Surgical System
3. [redacted]

Eyes with complications related to previous glaucoma interventions or cataract extraction (such as posterior capsular rent or vitreous presentation) should be exited from the study. The region where the trabeculotomy procedure is performed (e.g. superior hemisphere) and the extent of trabeculotomy should be recorded on the case report forms. [redacted]

Surgeons should follow their standard intra-operative and peri-operative medication regimen.

8.8 FOLLOW-UP VISITS

Follow-up visits should be performed according to the schedule provided in Table 1. All attempts should be made to conduct each follow-up visit within the time interval specified in Table 1. Evaluations conducted outside the prescribed time period will be considered protocol deviations.

NOTE: A safety IOP check anytime between the predefined visits (especially where the visits are sparse such as between 6 and 12 months) may be performed at the Investigator's discretion where warranted to ensure subject safety.

8.9 UNSCHEDULED VISITS

An unscheduled visit will be any visit to the clinical site, other than those specified in the protocol, at which the subject has a complaint regarding the study eye and/or treatment to the study eye is required or changed. The Investigator and/or qualified investigational staff will perform the procedures necessary to evaluate the study participant at these visits and will record the visit in the subject's medical records and on the CRF. No specific testing is required.

8.10 MANAGEMENT OF IOP AFTER SURGERY

In general, the primary consideration for the reintroduction of hypotensive medication is the preservation of the retinal nerve fiber layer, optic nerve and visual field. [redacted] Administration of glaucoma medication in subjects with IOP < 21 mmHg will be considered on a case-by-case basis by the study Investigator and the sponsor.

[redacted]

No more than one ocular hypotensive agent should be added at a single visit or within a 2-week period, without prior approval of the sponsor.

In the event of a steroid response increase in IOP due to prolonged anti-inflammatory regimen, the guidelines above to treat increase in IOP should be followed; however, topical hypotensive medications should be discontinued once the topical steroid has been discontinued.

Since the study population is undergoing angle surgery involving use of an ophthalmic viscoelastic agent, which is known to cause IOP spikes in some patients in the immediate postoperative period, use of glaucoma medications in the first month after surgery will be allowed at the discretion of the study Investigator. This short-term use of glaucoma medications in the immediate postoperative period will not be considered "rescue therapy" and will not be considered in the effectiveness analyses for the study.

For subject safety, a change in medical therapy may be implemented or additional surgical measures may be performed at any time during the study at the Investigator's discretion in the event it is required. The primary concern of the Investigator and

Sponsor at all times is the health and safety of the subjects. Usage of hypotensive medications specifically indicated for prevention of IOP spikes following Nd:YAG capsulotomy and administered for up to 72 hours after Nd:YAG capsulotomy will not be considered rescue therapy.

Medications which have been re-started by the Investigator may be discontinued if the Investigator's judgment is that the target intraocular pressure has been reached and the continued use of some or all of the therapy may not be required. Discontinuation of medications after re-introduction is recommended to be in the reverse order of re-introduction. The rationale for discontinuation should also be documented in the subject's medical record.

A record of all ocular hypotensive medications added, discontinued or changed will be documented on the appropriate CRF for each scheduled visit or on a CRF for an Unscheduled Visit, if necessary.

Another potential reason for intervention is hypotony. Intervention should only be considered if the hypotony has caused or is likely to cause sequelae such as a flat chamber or retinal detachment. No intervention is indicated when the vision is unchanged from screening, there is no persistent choroidal detachment, the anterior chamber is not flat with lens corneal touch, or the patient is asymptomatic. No intervention should be undertaken for hypotony which is not causing, or threatening to cause, a reduction in vision.

Secondary IOP-Lowering Interventions to Control IOP

If the subject requires another glaucoma procedure to control their IOP, the subject should continue to be followed according to standard of care until the adverse event resolves or 1-month post-re-intervention, whichever is longer. Following this, the subject should be withdrawn from the study.

Subjects who have had a secondary IOP-lowering intervention will be considered treatment failures for the purpose of the endpoint analyses. For the primary effectiveness endpoint of the study, the corresponding baseline unmedicated DIOP will be used to impute the 12-month unmedicated DIOP. These subjects will be included in the Safety Endpoint analyses through their withdrawal from the study.

8.11 WITHDRAWAL AND DISCONTINUATION

All subjects have the right to withdraw at any point during the study without prejudice. The investigator can discontinue any subject at any time at his/her discretion, or if continued participation in the study would result in harm to the subject. All efforts should be made by the investigator to retain the subject in the study. If a subject withdraws prematurely from the study, a genuine effort must be made to determine the

reason(s) the subject discontinued the study. The reason must be recorded in the subject's file and on the Study Exit Form.

8.12 SUBJECTS LOST TO FOLLOW-UP

Subjects who do not show up for a follow-up must be contacted to attempt to have them come for the follow-up. For those subjects who cannot be reached, every attempt to contact with the subject should be documented. If a subject misses two consecutive follow-up visits without any contact with the study staff, the subject will be considered lost-to-follow-up unless there is a further communication by the subject.

9 ADVERSE EVENTS (AES)

Adverse Events are defined below. Adverse events that occur in the eye during the trial, whether they are considered to be device related or not, must be documented in the subject's records. Date of the event, its severity, treatment (if any) and the assessed relationship of the event to the study device will be recorded on the Adverse Event Form. Conditions which exist at the time the subject is enrolled will be considered pre-existing conditions and do not need to be recorded as adverse events unless they increase in severity during the study. Sites should document any known existing medical and ophthalmic conditions at the time of screening.

9.1 DEFINITIONS OF AE, SAE, SADE, USADE

Adverse Event	Any untoward medical occurrence in a subject who has been treated with the device that does not necessarily have causal relationship with the treatment.
Adverse Device Effect	Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease that is possibly related to the study device.
Serious Adverse Event (SAE)	Any untoward medical occurrence that: • Results in death • Is life-threatening • Requires in-patient hospitalization or prolongs existing hospitalization • Necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure • Sight-threatening
Unanticipated Adverse Device Effect	Any serious adverse effect on health or safety, any life-threatening problem or death caused by, or associated with a device if that effect, problem, or death was not previously

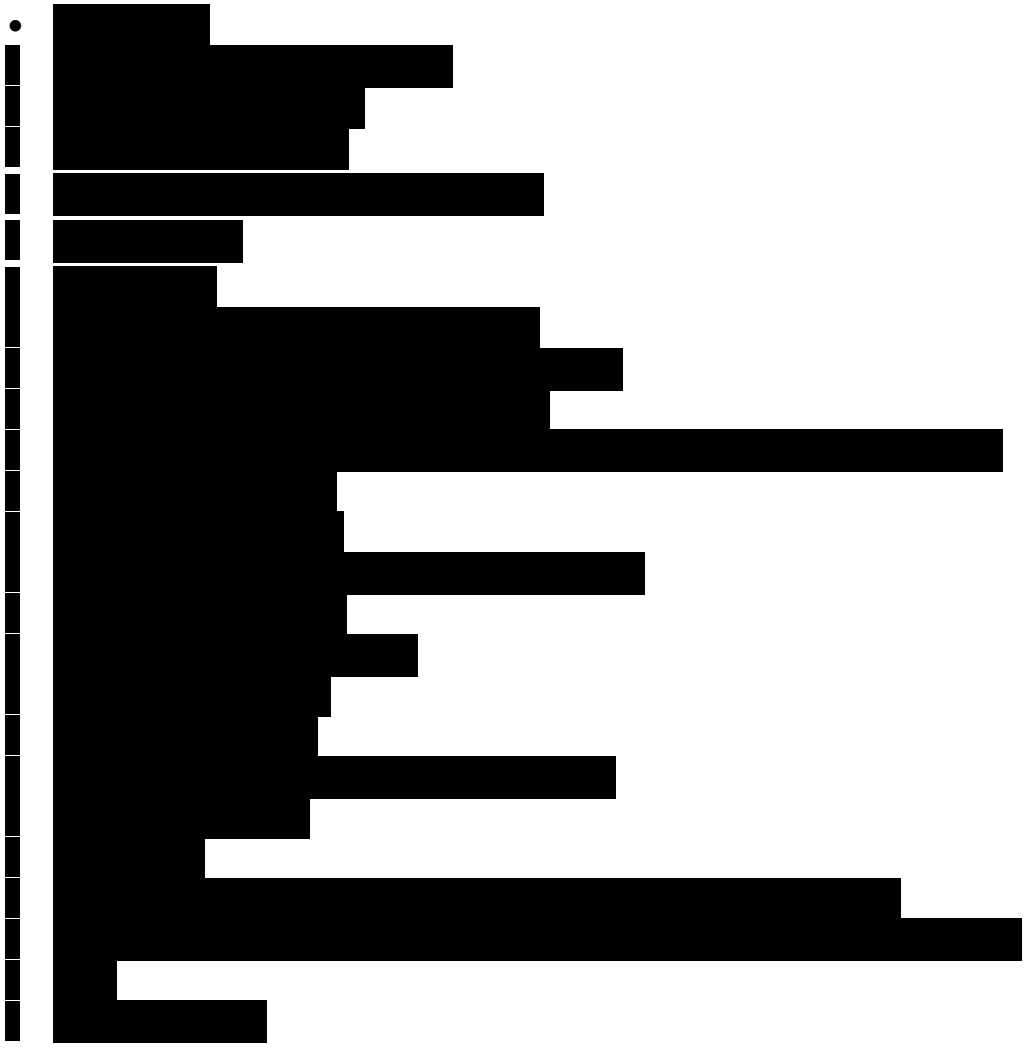
	identified in nature, severity, or degree of incidence in the clinical investigational plan; or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects (21 CFR 812.3(s)). Any sight-threatening event, whether listed in the protocol or not, is considered to be reportable as a UADE.

9.2 LIST OF ANTICIPATED POTENTIAL ADVERSE EVENTS

Anticipated potential adverse events listed below include those that might reasonably be expected to occur in this study because they are associated with glaucoma, ab-interno transluminal viscoelastic delivery, trabeculotomy, trabecular bypass stent, and/or the risk analysis for OMNI System. Adverse events may occur intra-operatively or post-operatively.

[22] To avoid double counting an event, events of IOP ≥ 10 mmHg above baseline IOP at ≥1 month visit that require management with systemic medication or secondary surgical intervention should be reported as "IOP increase requiring management with systemic medication at ≥1 month visit" or "Need for secondary surgery intervention to manage IOP," respectively.

[23] Hypotony is defined as "early" if it occurs within 2 weeks of surgery and "late" if it occurs more than 2 weeks after surgery



9.3 REPORTING ADVERSE EVENTS AND UNANTICIPATED ADVERSE DEVICE EFFECTS

Identification, collection and reporting of adverse event information is the responsibility of the principal investigator. The investigator records the date of the event, its severity, treatment (if any) and the assessed relationship of the event to the study device on the Adverse Event Case Report Form (AE CRF).

Any ocular **serious adverse event** (SAE) should be reported to the study sponsor within one business day of learning of the event. Non-ocular SAEs should be reported to the study sponsor within two working days of learning of the event. Email the AE CRF to

OMNIsafety@sightsciences.com and enter data in EDC system within two working days of learning of the event.

Any **unanticipated adverse device effects (UADE)** must be reported to the following two entities:

1. The study sponsor – Within one working day of the investigator first learning of the event, e-mail the AE CRF to OMNIsafety@sightsciences.com and enter data in EDC; and
2. The reviewing IRB – As soon as possible, but no later than 10 working days after the investigator first learns of the event, report per the IRB's instructions.

The sponsor will conduct an evaluation of unanticipated adverse device effects. If the sponsor determines that an unanticipated adverse device effect presents an unreasonable risk to subjects, parts of the investigation presenting risks will be terminated. Termination will occur no later than 5 working days after the sponsor makes such a determination and no later than 15 working days after the sponsor first received notice of the effect.

10 STATISTICAL CONSIDERATIONS

10.1 SAMPLE SIZE CALCULATION

The sample size calculation is based on the primary effectiveness endpoint, mean change in unmedicated DIOP from baseline at the 12-month postoperative examination. The study goal is to determine, in reducing the IOP in eyes with OAG undergoing cataract extraction, either OMNI (ab-interno transluminal viscoelastic delivery AND trabeculotomy) is superior [redacted], or OMNI (ab-interno transluminal viscoelastic delivery alone) is not inferior to the [redacted] in lowering the IOP with a non-inferiority margin of 1.5 mmHg. Due to the multiplicity, the significance level is adjusted to a two-sided significance level of 0.025 for each of the two hypotheses. The statistical hypotheses for the primary effectiveness endpoint are as follows:

Hypothesis I:
H_0: $\mu_{O2} = \mu_i$ versus H_a: $\mu_{O2} < \mu_i$, where μ_{O2} and μ_i are the mean change in unmedicated DIOP from baseline at the 12-month postoperative examination for the OMNI (ab-interno transluminal viscoelastic delivery AND trabeculotomy) and [redacted] groups, respectively. A negative mean change represents a mean reduction. The alternative hypothesis (H_a: $\mu_{O2} < \mu_i$) is to prove that the mean change in unmedicated DIOP of the OMNI (ab-interno transluminal viscoelastic delivery AND trabeculotomy) group is lower than that of the iStent inject group. In other words, the OMNI (ab-interno transluminal viscoelastic delivery AND trabeculotomy) is superior to the [redacted] group in lowering the IOP.

Hypothesis II:

H_0: $\mu_{O1} - \mu_i \leq -1.5$ mmHg versus H_a: $\mu_{O1} - \mu_i > -1.5$ mmHg, where μ_{O1} and μ_i are the mean change in unmedicated DIOP from baseline at the 12-month postoperative examination for the OMNI (ab-interno transluminal viscoelastic delivery alone) and [redacted] respectively. Since negative μ_{O1} and μ_i represent decreases in IOP, the alternative hypothesis (H_a: $\mu_{O1} - \mu_i > -1.5$ mmHg) is to prove that the mean change in unmedicated DIOP of the OMNI (ab-interno transluminal viscoelastic delivery alone) group is not worse than that of the [redacted] by 1.5 mmHg. In other words, the OMNI (ab-interno transluminal viscoelastic delivery alone) is not inferior to the [redacted] in lowering the IOP with a non-inferiority margin of 1.5 mmHg.

[redacted]

10.2 Analysis Populations

10.2.1 Safety Population

The safety analysis population will contain all randomized subjects wherein treatment is attempted. The attempt is defined as the OMNI device or [redacted] touching the study eyes even if the procedure is not completed. Subjects will be grouped according to actual treatments.

10.2.2 Intent to Treat (ITT) and As Treated (AT) Populations

The Intent to Treat (ITT) analysis population will include all subjects randomized and grouped according to randomization assignment (as randomized) regardless if the assigned procedure is performed. The As Treated (AT) population will consist of the subjects that undergo the assigned procedure and will be grouped according to actual treatments. For this study, the AT population will be used for the primary analyses of

the primary and other effectiveness endpoints. The effectiveness analyses may be performed for the ITT population if needed.

10.3 DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Subject demographics (age, race/ethnicity and gender) will be summarized by study group for the ITT, AT, and Safety populations using descriptive statistics. Age will be summarized as a continuous variable and categorized into the four groups based on the observed quartiles.

The baseline medicated IOP and washout (unmedicated) IOP will be summarized by study groups for the ITT and AT populations. They will be treated as continuous variables. The number of glaucoma medications in use at enrollment will be prepared for each of the study groups using descriptive statistics for categorical variables.

Medical and Ocular history will be summarized for each study group by number and percentage of subjects in the ITT and AT population.

For the Safety Population, ITT, and AT populations, subject accountability will be prepared based on Table G.1 of ANSI Z80.27-2014.

10.4 EFFECTIVENESS ENDPOINTS AND ANALYSIS METHODS

Descriptive statistics on continuous variables will include mean, standard deviation, median, minimum, and maximum. Confidence intervals for change from baseline will be included for selected endpoints. Categorical variables will be summarized using frequency counts and percentages. Exact confidence intervals for point estimates may be provided. Statistical testing will be one-sided with a significance level of 0.025 or two-sided significance level of 0.05 unless specify otherwise. Data listings of individual subject data may be provided.

10.4.1 PRIMARY EFFECTIVENESS ENDPOINT

The primary analysis of the primary effectiveness endpoint will be based on the AT population. The Baseline unmedicated DIOP will be used to impute the 12-month unmedicated DIOP for the subjects meeting any of the following criteria:

- Ocular hypotensive medications cannot be washed out properly at 12 months due to safety reasons.
- Have secondary surgical interventions (such as laser procedure or MIGS) to control IOP before the 12-month washout.
- Have any ocular procedures that can affect the IOP before the 12-month washout.

- Have IOP below 6 mmHg at 1 month or later
- Do not have the 12-month washed out DIOP due to any other reasons.

The change in unmedicated DIOP from baseline at 12 months will be calculated for each study eye as change = (12-month unmedicated DIOP – Baseline unmedicated DIOP).

The descriptive statistics (such as mean, standard deviation, median, minimum, and maximum) of the medication-free mean diurnal IOP and the change from baseline and the 95% confidence interval of the mean will be calculated for each of the three study groups. A two-sample t-test with a one-sided significance level of 0.025 will be used to compare the mean unmedicated DIOP change from baseline at 12 months for Hypotheses I and II described in Section 10.1. The two-sided 95% confidence interval based on the t-distribution will also be provided for the mean difference. In order to assess the pattern of the distribution, box-plots will be prepared for the medication-free mean diurnal IOP and its change from baseline for each of the three study groups.

10.4.2 SENSITIVITY ANALYSIS

A tipping-point analysis will be performed for the primary effectiveness endpoint. Let n and m be the number of OMNI and [redacted] subjects that do not have the 12-month washed out DIOP due to any reasons other than the first four criteria listed in Section 10.4.1. The tipping-point analysis for Hypothesis I in Section 10.1 will be performed as follows:

Let X_{O2} be the sample mean of the unmedicated DIOP change from baseline at 12 months for all OMNI (transluminal viscoelastic delivery AND trabeculotomy) subjects except for the n subjects and let X_i be that of the [redacted] *excluding the m subjects. Let ω and ν be the worst and best unmedicated DIOP change from baseline at 12 months observed from the subjects. The increment of 0.05 mmHg will be used in the tipping-point analysis. The first iteration in the tipping point analysis is to use X_{O2} to impute the missing values for the n subjects, use X_i to impute the missing values for the m subjects, and calculate the p-value of the statistical test described in Section 10.4.1. The second iteration is to use X_{O2} + 0.05 (i.e., worse than X_{O2}) to impute the missing values for the n subjects and X_i - 0.05 (i.e., better than X_i) to impute the missing values for the m subjects. The ith iteration is to use X_{O2} + 0.05 × i to impute the missing values for the n subjects and X_i – 0.05 × i to impute the missing values for the m subjects. The iterations will stop when the p-value becomes insignificant or the imputed value for the OMNI (transluminal viscoelastic delivery AND trabeculotomy) group is worse than the ω value or the imputation for the* [redacted] *is better than the ν value, which comes first. A figure of p-value as the Y-axis and iteration as the X-axis will be provided.*

The same tipping point analysis will also be performed for Hypothesis II in Section 10.1.

10.4.3 COVARIATE ANALYSIS

The following variables will be examined for their prognostic value to the primary effectiveness endpoint using the AT population with the imputation used for the primary analyses:

- Age group (based on observed quartiles)
- Gender (male and female)
- Race/ethnicity
- Baseline unmedicated DIOP group (based on observed quartiles)
- Number of ocular hypotensive medications at screening
- Study Site

For the primary effectiveness endpoint, two-way ANOVA with study group (three groups), one of the factors listed above, and the interaction between the study group and the factor will be used to check the possible covariate effects. A p-value of 0.15 will be used for evaluating the possible covariate effects. It should be noted that the subgroups of these covariates will be re-examined and may be re-categorized or eliminated due to small sample size (if there are < 10 subjects within each subgroup).

The scatter plots of the 12-month unmedicated DIOP versus the baseline unmedicated DIOP along with a 45º line will be provided. The scatter plot of the percent change in unmedicated DIOP from baseline to 12 months versus the baseline unmedicated DIOP will also be provided. The Box plots of the change and percent change in unmedicated DIOP from baseline to 12 months will be prepared for each category of the covariates (except for the study site).

10.4.4 OTHER IMPORTANT CLINICAL EFFECTIVENESS OUTCOMES

The statistical analyses for the other effectiveness endpoints will be based on the available data of the AT population. The percent change in unmedicated DIOP from baseline at 12 months will be calculated for each study eye as

% change = (12-month unmedicated DIOP – Baseline unmedicated DIOP) ÷ (Baseline unmedicated DIOP) × 100%.

The number and percent of subjects achieving $\geq$ 20% reduction in unmedicated DIOP from baseline at 12 months (i.e., 12-month responder) will be calculated. The exact 95% confidence interval of the 12-month responder rate will be calculated by the binomial distribution for each study group separately. The difference in the 12-month responder between OMNI (transluminal viscoelastic delivery AND trabeculotomy) and [redacted] groups and the corresponding 95% confidence interval per normal distribution will be calculated. The same statistics will be provided for the difference in the 12-month responder between OMNI (transluminal viscoelastic delivery) and [redacted] groups. The same statistical methods will be used to summarize the subjects with an unmedicated DIOP between 6 and 18 mmHg inclusive at 12 months.

The descriptive statistics for the continuous variables will be used to summarize the change in number of ocular hypotensive medications used from screening to 12 months. The ANOVA with study treatment group (three groups) as the factor will be used to compare the mean difference in the change in number ocular hypotensive medications used from screening to 12 months. The mean difference between OMNI (transluminal viscoelastic delivery AND trabeculotomy) and [redacted] and that between OMNI (transluminal viscoelastic delivery) and [redacted] will be evaluated using Dunnett's test. The same methods will be used to analyze the percent change in unmedicated DIOP from baseline to 12 months.

The analyses described in this section are exploratory in nature.

10.4.5 ADDITIONAL EFFECTIVENESS ANALYSES

The analyses described in this section are exploratory in nature. All the analyses will be based on the observed data of the AT population by the three study groups.

- Count and percent of subjects with the following DIOP change from baseline to 12 months stratified by the use of ocular hypotensive medication and/or SSI that can affect the IOP:
    - 40% ≤ Change (i.e. increase ≥ 40%)
    - 30% ≤ Change < 40% (i.e. 30% ≤ increase < 40%)
    - 20% ≤ Change < 30% (i.e. 20% ≤ increase < 30%)
    - 10% ≤ Change < 20% (i.e. 10% ≤ increase < 20%)
    - 0% < Change < 10% (i.e. 0% < increase < 10%)
    - Change = 0% (i.e. no change)
    - -10% < Change < 0% (i.e. 0% < decrease < 10%)
    - -20% < Change ≤ -10% (i.e. 10% ≤ decrease < 20%)
    - -30% < Change ≤ -20% (i.e. 20% ≤ decrease < 30%)
    - -40% < Change ≤ -30% (i.e. 30% ≤ decrease < 40%)
    - -50% < Change ≤ -40% (i.e. 40% ≤ decrease < 50%)
    - Change ≤ -50% (i.e. decrease ≥ 50%)
- Count and percent of subjects with the following DIOP 12 months stratified by the use of ocular hypotensive medication and/or SSI that can affect the IOP:
    - ≥6 mmHg to ≤ 21 mmHg
    - ≥6 mmHg to ≤ 18 mmHg
    - ≥6 mmHg to ≤ 15 mmHg
    - ≥6 mmHg to ≤ 12 mmHg
- IOP, IOP change, and IOP percent change from baseline at each visit (excluding use of ocular hypotensive medication and/or SSIs that can affect the IOP)
- The number of ocular hypotensive medications and change in the number of ocular hypotensive medications from screening to each post-operative

examination (including at 12 months prior to washout) excluding subjects treated with SSIs that can affect the IOP.

- The survival analysis (Kaplan Meier curve) with the log-rank test for the time to the first secondary surgery intervention (SSI) for controlling the IOP.
- The survival analysis with the log-rank test for the time to the first ocular hypotensive medications at or after 1 month postoperative. The analysis will include the cases with medications taken before 1 month and ongoing after 1 month.
- The survival analysis with the log-rank test for the time to the first SSI or the first ocular hypotensive medications at or after 1 month postoperative, whichever comes first.

10.5 SAFETY ANALYSIS

All safety analyses will be performed on the safety analysis population based on all available data by the three study groups separately.

10.5.1 ADVERSE EVENT

AE will be classified as pretreatment, intraoperative, or postoperative. The number and the percent of eyes reporting at least 1 AE of a given type will be summarized. Additionally, the number of reports of each type of AE will be provided.

Each AE will be summarized by incidence, percentage and the corresponding 95% confidence interval.

10.5.2 BEST CORRECTED VISUAL ACUITY (BCVA)

The number and percent of eyes reporting with BCVA of 20/20 or better, 20/25 or better, 20/32 or better, 20/40 or better, worse than 20/40 to 20/80, worse than 20/80 to 20/200, and worse than 20/200 at each visit will be summarized. The number and percent of eyes reporting BCVA of increase $\geq$ 10 letters, increase 10 letters, increase $\geq$ 5 letters to < 10 letters, within 5 letters change, decrease $\geq$ 5 letters to < 10 letters, decrease 10 letters, and decrease $\geq$ 10 letters at each postoperative visit will be calculated.

10.5.3 OTHER SAFETY OUTCOMES

The number and percent of eyes reported with each kind of slit lamp findings, gonioscopy findings, and dilated fundus examination findings at each visit will be provided.

The descriptive statistics for the continuous variables will be derived for the visual field mean deviation (MD) and pattern standard deviation (PSD).

10.6 INTERIM ANALYSIS

An interim analysis providing descriptive statistics for the outcomes may be completed following completion of the Month 6 follow-up visit by 80% of the randomized subjects. Endpoints listed below will be analyzed at an interim analysis. No device effectiveness will be claimed based on the interim analysis outcomes.

Effectiveness outcomes up to 6 months will be summarized descriptively:

1. Percent of eyes with a ≥20% reduction in IOP with no increase in IOP-lowering medications compared to screening visit
2. Percent of eyes with IOP between 6 and 18 mmHg with no increase in IOP-lowering medications compared to screening visit
3. Percent of eyes with IOP between 6 and 21 mmHg with no increase in IOP-lowering medications compared to screening visit
4. Reduction in mean IOP from screening visit; and
5. Reduction in mean number of IOP-lowering medications from screening visit for the subjects who are on medications at the screening visit

Safety endpoints:

1. Rates of ocular adverse events (intraoperative, postoperative)
2. Reduction in best corrected visual acuity (BCVA) from baseline (note: reduction in BCVA due to PCO will not be treated as a safety event)

10.7 DEVIATION FROM THE STATISTICAL PLAN

Any deviations from the statistical plan will be noted in the final report.

11 MONITORING PROCEDURES

Sight Sciences or contract research organization (CRO) personnel will monitor the study in a manner consistent with FDA regulations, good clinical practices and the clinical research standards adopted by Sight Sciences. Study monitoring will be executed using on-site and remote monitoring visits. Study monitoring will involve the following elements:

- Site Qualification: Sight Sciences or CRO personnel will meet with investigators and clinical study staff prior to the initiation of the study in order to review the adequacy of the subject population, facilities, and equipment with respect to the needs of the study, and to familiarize the investigator with the study protocol. If Sight Sciences or the CRO have recently been involved with an investigator for another study, a site qualification visit may not be necessary.

- Site Initiation: Sight Sciences and/or CRO personnel will meet with the investigator(s) and clinical study staff when the site is ready to begin enrolling subjects in order to train them in how to properly select subjects, perform the study procedure, and record study data. This visit will include, but not be limited to a review of the following:
  - Detailed review of the protocol
  - Informed consent procedures
  - Instructions for the surgical procedure
  - Records and reports
- Interim Monitoring: Sight Sciences or CRO personnel will conduct routine visits during the course of the study to review charts, perform source document verification, ensure proper adherence to the study protocol, and to review regulatory documents. Interim monitoring visits and telephone consultation will occur as necessary during the course of the study to ensure the proper progress and documentation of the study findings.
- Study Close Out Visit: At the conclusion of the trial there will be a study closure visit during which several actions, including but not limited to the following, will be performed:
  - A final inspection of the study binder
  - Accountability and return of all devices and non-consumable ancillary study supplies to the sponsor
  - Discussion of record retention requirements with the investigator
  - Close-out notification to the IRB

12 DATA AND QUALITY MANAGEMENT

12.1 DATABASE MANAGEMENT

The study database will be designed using an electric data capture (EDC) system that is compliant with 21 CFR Part 11 and relevant guidance documents. The EDC will be developed and maintained by an independent, qualified data management firm.

The database will incorporate time-stamped audit trails, protection of human subjects, restricted access, and data security at the component level. Each database module, including each individual eCRF, will be validated by conducting a series of standard tests that demonstrate usability and correctness of the database system. The database will be maintained on an ongoing basis and will be routinely backed up.

12.2 SUBJECT IDENTIFICATION

The subjects will be identified by a six-digit subject number composed of a double-digit study identification number, a two-digit center identification number followed by a three-digit sequential subject number. A subject identification number will be assigned

after informed consent is obtained. This will ensure that identifiable subject information has been removed and kept confidential.

12.3 SUBJECT ACCOUNTABILITY

All subjects enrolled and treated in this clinical investigation shall be monitored for the duration of the investigation. The clinical investigation shall be considered completed when all subjects that have been enrolled in the investigation have reached the final reporting period, excluding subjects who were withdrawn.

12.4 CONFIDENTIALITY

All medical records associated with the clinical investigation will be made available for review by Sight Sciences personnel, its contract research organization (CRO) and governmental/regulatory agencies involved. The results of the study may be published in the future for scientific and marketing purposes, but the identity of each subject will not be revealed. All records will be stored in a secure area at the investigator's facility, the CRO, the data management firm and at Sight Sciences, Inc.

12.5 SOURCE DATA AND CASE REPORT FORMS

Source data will be entered into a validated electronic system at each site by trained personnel in accordance with 21 CFR Part 11 requirements. Electronic entries will be verified against corresponding source data at the sites and queried/corrected if needed to the extent possible. Medical site records serve as source data. In addition, data that are collected exclusively for the purpose of this study and not normally recorded in the subjects' medical records can be collected directly on any study CRFs or tools provided by the sponsor, and these will serve as the source data.

Source data and study CRFs are to be maintained at the site in the subject records or in the medical records. All data entries must be made in accordance with ALCOA (**A**ttributable, **L**egible, **C**ontemporaneous, **O**riginal, **A**ccurate) standards and GDP (Good Documentation Practices).

Study data acquired from sites will be collected on Electronic Case Report Forms (eCRFs) for submission to sponsor. Sites will enter data entered on source documents into the electronic case report forms for Sponsor review and analysis.

12.6 RETENTION PERIOD

Clinical sites are to retain any and all clinical trial material (documentation, photographs, etc.) for a period of two years from the date a marketing application is approved or two years after the investigation has been discontinued, or as directed by their institutional document retention requirements, whichever is the longest. After that time, the items must be returned to Sight Sciences for archiving.

13 PROTOCOL MODIFICATIONS AND DEVIATIONS

Protocol modifications may occur during the study. Each will be approved by the sponsor before implementation. Each will undergo Institutional Review Board (IRB) review and approval, as necessary.

Any deviations from this protocol intended to protect the life or physical well-being of a subject in an emergency are to be reported to Sight Sciences, Inc. as well as the IRB as soon as possible, and no later than 5 working days after the emergency occurred.

All protocol deviations will be documented using the Protocol Deviation CRF or Source Tool.

14 DEVICE FAILURES AND MALFUNCTIONS

All study device failures (OMNI surgical system) or malfunctions should be recorded on the Customer Experience Form and reported to Sight Sciences Customer Service (877-266-1144).

15 ETHICAL CONSIDERATIONS

15.1 DECLARATION OF HELSINKI

This study shall be conducted in accordance with the Declaration of Helsinki (Appendix D).

15.2 INSTITUTIONAL REVIEW BOARDS (IRB)

The study shall not begin at a site until approval has been obtained from the reviewing IRB. It is the Investigators' responsibility to obtain and maintain written approval of the study protocol and Informed Consent documents from the appropriate IRB. It is also the Investigators' responsibility to notify that body about any amendments to these documents and to follow the IRBs rules regarding the reporting of Adverse Events and Protocol Deviations related to the device and/or this study. Copies of all written approvals (identifying the study, the submitted and approved documents and the date reviewed) and the approved versions of the documents must be provided to Sight Sciences or its CRO.

The Investigators must file all correspondence with the IRB and forward copies of such correspondence to Sight Sciences.

15.3 INFORMED CONSENT DOCUMENT (ICD)

An Informed Consent template that covers all protocol procedures and follows GCP Guidelines will be prepared by Sight Sciences and made available to each Investigator. The Investigator may adapt these templates to the requirements of the local IRB and of the institution where the study is conducted, but any revisions made to the ICD must be submitted to the sponsor for review prior to submission to the IRB. A copy of each IRB-approved ICD version is to be made available to Sight Sciences and its CRO. The approved, IRB-stamped ICD is to be kept in its full length in the study Regulatory Binder. Original, signed ICDs are to be maintained in study records and must be made available for monitoring review.

15.4 PUBLIC LISTING OF STUDY

The study will be listed on the NIH website www.clinicaltrials.gov.

16 STUDY ADMINISTRATION

16.1 EARLY TERMINATION OR SUSPENSION OF THE STUDY OR AN INVESTIGATIONAL SITE

Sight Sciences may terminate the study, in which case the investigators and associated IRBs will be notified in writing. Possible reasons for study termination include but are not limited to:

- The discovery of an unexpected, significant, or unacceptable risk to the study subjects implanted with the device
- Withdrawal of FDA clearance of the OMNI device.
- Insufficient enrollment in the study
- The Sponsor determines that enough data has been collected for the study, and no further data are needed.

Sight Sciences reserves the right to stop the study at a particular site any time after the initiation visit if there have been no subject enrollments or if there have been significant protocol deviations/violations at the site.

Likewise, a principal investigator may terminate the study at his/her institution. This decision must be followed by written notification to Sight Sciences within five working days, stating the reasons for termination.

If the study is terminated, every effort should be made to obtain final follow-up from all subjects.

In the event that there are significant human use issues with the device, the investigator will be consulted to make a determination of whether the study should be terminated or not.

16.2 INVESTIGATOR RESPONSIBILITIES

16.2.1 GENERAL RESPONSIBILITIES OF INVESTIGATORS

An Investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of subjects under the Investigator's care, and for the control of devices under investigation. An Investigator also is responsible for ensuring that informed consent is obtained in accordance with 21 CFR part 50.

16.2.2 SPECIFIC RESPONSIBILITIES OF INVESTIGATORS

1. Awaiting approval - An Investigator may determine whether potential subjects would be interested in participating in an investigation but shall not request the written informed consent of any subject to participate, and shall not allow any subject to participate before obtaining IRB approval.
2. Subject Qualification -The Investigator is responsible for ensuring that all subjects entering the study conform to the subject selection criteria.
3. Compliance - An Investigator shall conduct an investigation in accordance with the signed agreement with the Sponsor, the investigational plan, all applicable FDA regulations, and any conditions of approval imposed by an IRB.

16.2.3 INVESTIGATOR RECORDS

A participating Investigator shall maintain the following accurate, complete, and current records relating to the Investigator's participation in an investigation for the period specified in Section 12.6:

1. All correspondence with another Investigator, an IRB, the Sponsor, a clinical research associate (CRA) or monitor, or FDA, including required reports.
2. Records of each subject's case history and exposure to the device. Case histories include the subejct's study clinic record, certified copies of medical record as applicable, and supporting documents including, signed and dated consent forms. Such records shall include:
    a) Documents evidencing informed consent.
    b) All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation,

including information about relevant previous medical history and the results of all diagnostic tests.

3. The protocol, with documents showing the dates and reasons for each deviation from the protocol.
4. Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

16.2.4 INVESTIGATOR REPORTS

An Investigator shall prepare and submit the following complete, accurate, and timely reports:

1. Unanticipated Adverse Device Effects - An Investigator shall submit to the Sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the Investigator first learns of the effect.
2. Withdrawal of IRB Approval - An Investigator shall report to the Sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the Investigator's part of an investigation.
3. Progress - An Investigator shall submit progress reports on the investigation to the Sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.
4. Deviations from the Investigational Plan - An Investigator shall document and report to the Sponsor any deviation from the investigational plan.
5. Informed Consent - If an Investigator enrolls a subject without obtaining informed consent, the Investigator shall report such use to the Sponsor and the reviewing IRB within 5 working days after the use occurs.
6. Final Report - An Investigator shall, within 3 months after termination or completion of the investigation or the Investigator's part of the investigation, submit a final report to the Sponsor and the reviewing IRB.
7. Other - An Investigator shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

16.3 INVESTIGATOR AGREEMENT

The principal investigators in each center shall agree to the clinical protocol and any amendments and indicate their approval and agreement by signing and dating the cover page of the study protocol and the Investigator Responsibility Agreement.

17 PUBLICATION POLICY

Sight Sciences recognizes the value of disseminating research results. It is understood that the Study is part of the Multi-Center Clinical Trial and publication of results is expected. This publications policy applies to journal articles, conference abstracts, and conference presentations (posters and slides) covering Sight Sciences-sponsored clinical studies. This policy is in addition to any arrangement contained in the Clinical Trial Agreement between Sight Sciences and the investigator.

Multi-Site Data

Clinical site investigators are encouraged to propose publications and abstracts that include clinical or research data from multiple clinical sites; such projects will be coordinated by Sight Sciences. Authorship of papers and abstracts resulting from these projects will be determined collaboratively according to the following guidelines:

- The first author on such publications will be the person who primarily wrote the paper and took the lead on the research. In the case of clinical trial papers where all authors contributed equally, authorship order may be based on site enrollment or other criteria at Sight Sciences' discretion.
- Other authors include those who significantly contributed to the specific work.
- At least one person from each clinical site whose study subjects appear in the work will be acknowledged in the manuscript/presentation in some way, either as an author group member, a non-author contributor, or listed in the acknowledgements, depending on the particular policies of the journal or conference.

Single Site Data

After publication of the multi-center study results in a peer-reviewed journal, or if Sponsor has not submitted a manuscript for publication in a peer-reviewed journal within twelve (12) months after the study has been completed, whichever occurs first, Investigators may publish the results of the Study generated by the Investigator, subject to the obligations of the Clinical Trial Agreement between Sight Sciences and the Investigator, and the prior approval of Sponsor in writing.

Publications Review Policy

Investigators must submit all presentations, posters, abstracts and manuscripts pertaining to this study to Sight Sciences for review in advance of their submission. Sight Sciences conducts this review to protect its proprietary rights to information, inventions, or products developed under the Study. Please use the following guideline to determine the absolute minimum advance time for submitting an item to Sight Sciences for review:

- Presentations/Posters: 5 business days in advance of presentation

- Abstracts: 5 business days in advance of submission
- Manuscripts: 30 calendar days in advance of submission for publication

In accordance with the Clinical Trial Agreement, these items must receive written approval from Sight Sciences in order for them to be submitted or presented. If an item is not received in the timeframe listed above, approval may not be granted due to insufficient time for considered review. In addition, since most of our Clinical Trial Agreements require that Sight Sciences has 60 days to review publications, Sight Sciences reserves the rights granted in those Agreements if circumstances require a longer review.

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19 APPENDIX A – METHODS FOR EXAMS, TESTS AND QUESTIONNAIRES

19.1 LIST OF STUDY PROCEDURES

1. Informed Consent
2. Demographics, Medical & Ocular History
3. Medication Log
4. Patient-Reported Outcomes (PROs): OSDI and GQL-15
5. BCVA ETDRS
6. Visual Field (Humphrey 24-2 SITA- Standard)
7. IOP (Goldmann Tonometry)
8. Unmedicated Diurnal IOP
9. Gonioscopy
10. Slit Lamp Exam
11. Dilated Fundus Exam/C:D Ratio
12. Eligibility Assessment
13. Randomization
14. Surgical procedure
15. AE Assessment

19.2 PRO INSTRUMENTS

19.2.1 THE OSDI© QUESTIONNAIRE

The OSDI Questionnaire consists of 12 questions regarding ocular symptoms, environmental triggers, and vision-related functioning in patients with dry eye disease (Schiffman et al, 2000). The patient will be asked to rate each symptom using a 5-point scale (0 to 4), where 0 indicates none of the time; 1, some of the time; 2, half of the time; 3, most of the time; and 4, all of the time. Seven questions related to visual functioning allow a response of "N/A" (not applicable); no more than 3 of these 7 questions may be answered as N/A for the questionnaire to be evaluable. The total OSDI score is calculated as: ([sum of scores for all questions answered] X 100)/([total number of questions answered] X 4).

19.2.2 THE GQL-15 QUESTIONNAIRE

The GQL-15 questionnaire was developed by Nelson et al and is comprised of 15 vision-related items. The item-level responses for each factor are coded on a five-point scale (1 meaning no difficulty and 5 meaning severe difficulty), while 0 is marked if the participant does not perform the activity as a result of non-visual cause. These items are grouped into four subscales: 1) "Central and near vision" (two items); 2) "Peripheral vision" (six items); 3) "Dark adaptation and glare" (six items); and 4) "Outdoor mobility" (one item). Total score is derived by summing all item-level response scores. Higher GQL-15 scores are revealing lower QOL. Subscale scores are derived by coding the item-level responses on a numerical interval scale ranging from 0 (no difficulty) to 100 (severe difficulty). Subscale scores are average of the sum of scores generated for the item-level subscale responses. Higher subscale scores are indicating lower QOL and greater difficulty with subscale specific tasks.

19.3 VISUAL ACUITY WITH MANIFEST REFRACTION

ETDRS will be used in testing and documenting subject visual acuity.

ETDRS Testing Method
Best-corrected visual acuity (BCVA) will be tested and scored using the ETDRS system, and will be obtained at the screening and baseline visits for both eyes, and at all scheduled follow-up visits for the study eye only.

The ETDRS chart must be placed at a distance of 4.00 meters (13 feet and 1.5 inches, or 157.5 inches) from cornea to chart surface, when using a 4-meter chart. For the patients unable to read the topmost line of 4.00 meter chart VA should be tested at 1 meter. For testing at 1 meter, the distance must be 1.00 (39 and 3/8 inches).

The 1-meter distance is measured from the eye of the participant, seated comfortably in a chair with his/her back firmly placed against the chair, to the center of the 2nd or 4th letter of the 3rd line of the chart. The measuring device can be homemade (e.g., a dowel rod accurately cut to a length of 1.00 m) or 1 meter ruler may be purchased.

Note: If it is necessary to refract at the 1-meter distance, a +0.75 sphere lens should be added to the trial frame. Subtract the +0.75 sphere from the final refraction obtained at the 1-meter distance before recording the refraction on the form.

Methods

The subject should attempt to read each letter, line-by-line, left to right, beginning with line 1 at the top of the chart. The subjects should be told that the chart has letters only, no numbers. If the subject reads a number, he or she should be reminded that the chart contains no numbers, and the examiner should then request a letter in lieu of the number. The subject should be asked to read slowly, about one letter per second, so as to achieve the best identification of each letter. He/she is not to proceed to the next letter until he/she has given a definite response.

A maximum effort should be made to identify each letter on the chart. When the subject says he/she cannot read a letter, the subject should be encouraged to guess. If the subject identified two (2) letters (e.g., A or B), the subject should be asked to choose one letter and, if necessary, to guess. When it becomes evident that no further meaningful readings can be made despite encouragement to read or guess, the examiner should stop the testing for that eye. However, all letters on the last line should be attempted as letter difficulties vary and the last letter may be the only one read correctly. The number of letters read correctly should be recorded.

In order to provide a standardized and well-controlled assessment of visual acuity, visual acuity assessments for all subjects should be performed under consistent conditions (e.g., the same lighting conditions, viewing distance, etc.) at each visit.

19.4 MEASUREMENT OF INTRAOCULAR PRESSURE

Goldmann tonometer should be used each time IOP is measured. To minimize observer bias, follow a reader-operator technique to measure and record the IOP; the individual operating the tonometer (operator) should not view the dial during the measurement. A separate individual (reader/recorder) should view the dial and note the measurement. Take two measurements of IOP. If the measurements differ by more than 2 mmHg, take a third measurement. If two measurements are taken, record the mean on the case report form. If three measurements are taken, record the median on the case report form.

At all scheduled visits every attempt should be made to have these measurements taken at the same time interval to minimize the effect of daily fluctuations in pressure.

Guidelines for performing Goldmann tonometry are as follows:

1. The subject is told the purpose of the test and is reassured that the measurement is not painful. The subject is instructed to relax, maintain his or her position, and hold his or her eyes open widely.
2. One drop of a topical anesthetic, such as 0.5% proparacaine or 0.4% benoxinate, is placed in each eye, and the tip of a moistened fluorescein strip is touched to the tear layer on the inner surface of each lower lid. Alternatively, one drop of a combined anesthetic-fluorescein strip is touched to the tear layer on the inner surface of each lower lid. The tonometer and prism are set in correct position on the slit lamp.
3. The tension knob is set at 1 g. If the knob is set at 0, the prism head may vibrate when it touches the eye and damage the corneal epithelium. The 1 g position is used before each measurement. As a rule, it is more accurate to measure intraocular pressure by increasing rather than decreasing the force of applanation.
4. The 0 graduation mark of the prism is set at the white line on the prism holder. If the subject has more than 3 diopters of corneal astigmatism, the area of contact between the cornea and the prism is elliptic rather than circular. In this situation the prism should be rotated to 45 degrees from the long axis of the ellipse-that is, the prism graduation corresponding to the least curved meridian of the cornea should be set at the red mark on the prism holder. An alternative approach is to average the intraocular pressure readings obtained with the axis of the prism horizontal and then vertical.
5. The cobalt filter is used with the slit beam opened maximally. The angle between the illumination and the microscope should be approximately 60º. The room illumination is reduced.
6. The subject is seated in a comfortable position on an adjustable stool or examining chair facing the slit lamp. The heights of the slit lamp, chair and chin rest are adjusted until the subject is comfortable and in the correct position for the measurement. The subject's chin is supported by the chin rest and the forehead by the forehead bar. The forehead bar should be well above the subject's eyebrows so the frontalis muscle can be used to open the eyes widely. The subject's collar and tie should be loosened if necessary. The subject should breathe normally during the test to avoid Valsalva's maneuver.
7. The palpebral fissure is a little wider if the subject looks up. However, the gaze should be no more than 15° above the horizontal to prevent an elevation of intraocular pressure that is especially marked in the presence of restrictive neuromuscular disease. A fixation light may be placed in front of the fellow eye. The subject should blink his eyes once or twice to spread the

fluorescein-stained tear film over the cornea and then should keep his eyes open widely. In some subjects it is necessary for the examiner to hold the eyelids open with the thumb and forefinger of one hand. Care must be taken not to place any pressure on the globe because this raises intraocular pressure.

8. The operator sits opposite the subject in position to look through the microscope. The clinician moves the assembly toward the subject. When the black circle near the tip of the prism moves slightly, it indicates contact between the prism and the globe.
9. Alternatively, the assembly is advanced toward the subject until the limbal zone has bluish hue. The biprism should not touch the lids or lashes because this stimulates blinking and squeezing. Touching the lids also thickens the fluorescein rings, which may cause an overestimation of intraocular pressure.
10. The clinician observes the applanation through the biprism at low power. A monocular view is obtained of the central applanated zone and the surrounding fluorescein stained tear film. Using the control stick, the observer raises and lowers and centers of the assembly until two equal semicircles are seen in the center of the field of view. If the two semicircles are not equal in size, intraocular pressure is overestimated. The clinician turns the tension knob in both directions to ensure that the instrument is in good position. If the semicircles cannot be made "too small," the instrument is too far forward. If the semicircles cannot be made "too large," the instrument is too far from the eye.
11. The fluorescein rings should be approximately 0.25 to 0.3 mm in thickness, that is, one tenth the diameter of the flattened area. If the rings are too narrow, the subject should blink two or three times to replenish the fluorescein; additional fluorescein may be added if necessary. If the fluorescein rings are too wide, the subject should dry his eyes lightly with a tissue, and the front surface of the prism should be dried with lint-free material. An excessively wide fluorescein ring is less of a problem than a very narrow ring but can cause the intraocular pressure to be overestimated.
12. The fluorescein rings normally undergo a rhythmic movement in response to the cardiac cycle. The tension knob is rotated until the inner borders of the fluorescein rings touch each other at the midpoint of their pulsations. The intraocular pressure is the mean of these 2 readings.
13. Intraocular pressure is measured in the study eye twice. If the 2 readings differ by 2 mmHg or less the average is the IOP. If the 2 readings differ by > 2 mm Hg, a third reading is taken.
14. The reading obtained in grams is multiplied by 10 to give the intraocular pressure in millimeters of mercury. This value is recorded along with the date, time of day, list of ocular medications, and time of last instillation of ocular medication if IOP is measured on different days, an attempt should be made to standardize the time.

Errors in measurement can arise from a number of factors, including the following:

1. Inadequate fluorescein staining of the tear film causes an underestimation of intraocular pressure.
2. Elevating the eyes more than 15° above the horizontal causes an overestimation of intraocular pressure. Widening the lid fissure excessively causes an overestimation of intraocular pressure.
3. Repeated tonometry reduces intraocular pressure, causing an underestimation of the true level. This effect is greatest between the first and second readings, but the trend continues through a number of repetitions.
4. A scarred, irregular cornea distorts the fluorescein rings and makes it difficult to estimate intraocular pressure.
5. The thickness of the cornea affects intraocular pressure readings. If the cornea is thick because of edema, intraocular pressure is underestimated. If the cornea is thick because of additional tissue, intraocular pressure is overestimated. The Goldmann tonometer is accurate after epikeratophakia.
6. If the examiner presses on the globe or if the subject squeezes his eyelids, intraocular pressure is overestimated.
7. If corneal astigmatism is greater than 3 diopters, intraocular pressure is underestimated for with the rule astigmatism and overestimated for against the rule astigmatism. The intraocular pressure reading is inaccurate 1 mm Hg for every 3 diopters of astigmatism.

Calibration and Documentation

The calibration of the tonometer will be checked at least once every three months with the weight system at 0, 2, and 6 grams as supplied by the manufacturer. When the calibration steps provide readings within ± 2 mmHg of the target value for each weight, the tonometer is considered adequately calibrated. However, if the variation exceeds this amount, a different adequately calibrated instrument should be used for IOP measurements.

The investigator must maintain written documentation in a log (hardcopy or electronic format acceptable) of the calibration of each tonometer used at the beginning and throughout the study period and make these records available to study monitors for review. Documentation must describe the unit (by model and serial number or other permanent identifier), the date of each calibration, the name or initials of the person performing the calibration, and an indication as to whether or not the unit passed the calibration. If not calibrated successfully, a note should be entered in the log about contacting the authorized manufacturer's representative for repair and what repairs were required. Following any repair, another calibration should be documented prior to clinical use.

Diurnal IOP
In order to determine the mean diurnal intraocular pressure (IOP) measurements at baseline and 12 months, IOP measurements should be taken at 9:00AM ±1.5 hours, 12:00PM ± 1 hour, and 4:00PM ± 2 hours. The three IOP measurements should then be averaged to determine the mean diurnal IOP.

19.5 VISUAL FIELD EXAMINATION

Visual fields must be automated threshold visual fields, 24-2 Humphrey Stimulus III. The SITA Standard must be used for the visual field conducted at the pre-operative evaluation and all subsequent evaluations. Visual fields should be reliable as determined by the Investigator. A visual field done within 6 months prior to the subject informed consent date and in accordance with the 24-2 SITA Standard requirements can be used for the baseline evaluation. For visual fields that do not meet the reliability standards, the test should be repeated within two weeks.

Visual fields are to be performed with a non-dilated pupil unless, in the opinion of the investigator, the pupil is so miotic that dilation is required (e.g., < 3mm). If dilation was performed at screening, it should be performed at all subsequent visual field examinations. However, dilation should not be performed before the IOP measurement on the appropriate visits.

It is recommended that the following set up occur for the visual field:
SITA Standard 24-2 test

- using the white, size III stimulus,
- Foveal Threshold ON,
- Head Tracking ON and
- Vertex Monitoring OFF.

The appropriate trial lens as defined by the perimeter should be used.

19.6 DILATED FUNDUS EXAMINATION

A mydriatic should be used to dilate the pupil so that an examination of the fundus can be conducted with an indirect ophthalmoscope and slit lamp biomicroscopy (with contact lens, Hruby lens or 60-, 66-, 78-, or 90 diopter lens). The appearance of the optic disc, macula, vessels and periphery should be evaluated and reported on the Baseline form. A measurement of the cup to disc ratio should be made and reported.

19.7 SLIT LAMP EXAMINATION

The clinician will examine the conjunctiva, cornea, anterior chamber, lens and anterior vitreous of the eye with the aid of a slit lamp, which is a table-mounted binocular microscope. Fluorescein dye will be instilled into the ocular cul-de-sac to facilitate this

examination. In addition to the following, any evidence of pigment dispersion visible in slit lamp examination should be evaluated and noted.

Iris

Findings of Atrophy/Erosion; Peaking; and Rubeosis should be noted. Each will be evaluated using a scale of None (0), Mild (+1), Moderate (+2) and Severe (+3).

Cornea - Edema

None (0)	Transparent and clear or less than mild
Mild (+1)	Dull glassy appearance
Moderate (+2)	Dull glassy appearance of epithelium with large number of vacuoles
Severe (+3)	Epithelial bullae and/or stromal edema, localized or diffuse, with or without stromal striae

Cornea - Staining/Erosion

None (0)	No fluorescein staining of epithelium, OR less than mild
Mild (+1)	Slight fluorescein staining confined to a small focus
Moderate (+2)	Regionally dense fluorescein staining (1 mm or greater in diameter) with underlying structure moderately visible
Severe (+3)	Marked fluorescein staining or epithelial loss

Anterior Chamber

The following system is recommended for grading of aqueous cells and flare using a slit beam 1.0 mm wide and 1.0 mm long.

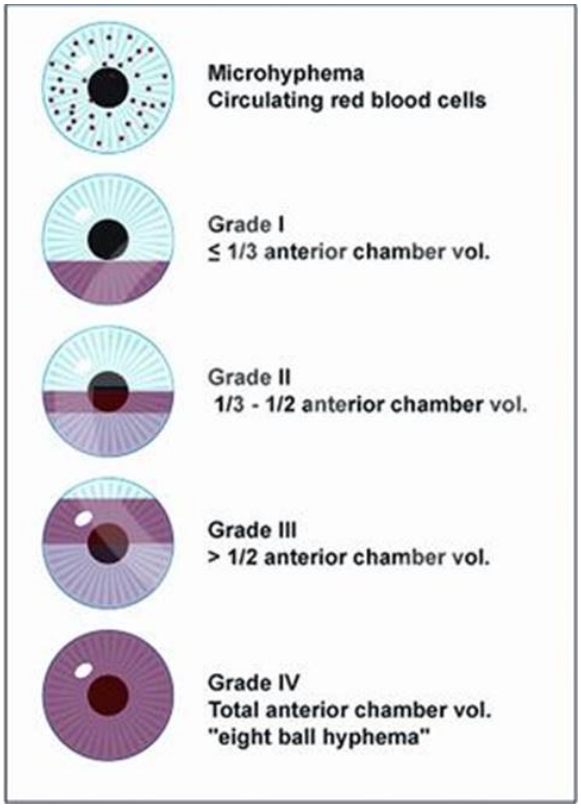
Cells

0 = < 1 cell seen
0.5+ = 1-5 cells seen
1+ = 6-15 cells seen
2+ = 16-25 cells seen
3+ = 26-50 cells seen
4+ = > 50 cells seen

Flare

0 = None
1+ = Faint
2+ = Moderate (iris and lens details clear)
3+ = Marked (iris and lens details hazy)
4+ = Intense (fibrin or plastic aqueous)

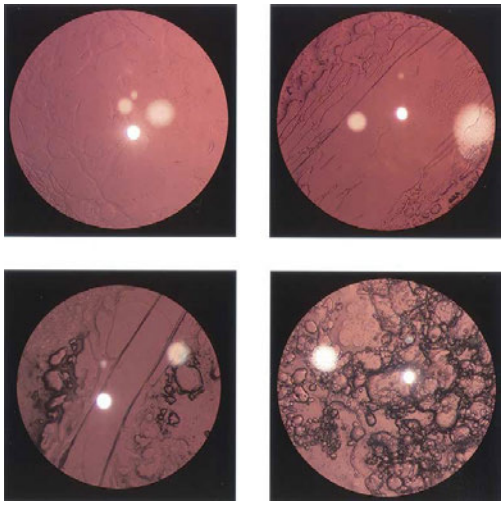
The presence of hypopyon is recorded separately. The presence of "microhyphema" or "layered hyphema" in the anterior chamber should also be recorded. Layered hyphema will be graded using the following scale (If Grade 1, also record size in mm on the CRF).[24]



[24] http://www.aao.org/image/hyphema-grading-system-2

Posterior Capsule Opacification

As a routine part of the slit lamp examination, posterior capsule opacification (PCO) will be evaluated using the following scale:



NONE

Minimal (Top left image)

Mild (Top right image)

Moderate (bottom left image)

Severe (bottom right image)

Other Slit Lamp Findings (complete for each finding)

- Trace
- Mild
- Moderate
- Severe

19.8 GONIOSCOPY

Gonioscopy will be conducted as part of the screening process to verify that the subject has an open angle and to identify any anterior synechiae as well as determine if there is any pigment dispersion. Gonioscopy will be repeated post-operative follow up visit as per Table 1. A Zeiss, Sussman or similar lens should be used and gonioscopy conducted in a dark room with a narrow, short slit beam that does not pass through the pupil and without a fixation light being used. The Shaffer method will be used as follows: grade 4, wide open (35°-45°): grade 3, moderately open (25°-34°); grade 2, moderately narrow (20°); grade 1, very narrow (10°); grade 0, closed (0°). The grade number will be reported for each quadrant of the eye in the appropriate location on the form.

19.9 OCULAR HYPOTENSIVE MEDICATIONS

Each ocular hypotensive medication will be recorded on the study record. If subjects are taking combination medications such as Cosopt this is to be counted as two medications even though this is only in 1 bottle.

20 APPENDIX B - DECLARATION OF HELSINKI

I. PREAMBLE

1. The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data.

   The Declaration is intended to be read as a whole and each of its constituent paragraphs should be applied with consideration of all other relevant paragraphs.

2. Consistent with the mandate of the WMA, the Declaration is addressed primarily to physicians. The WMA encourages others who are involved in medical research involving human subjects to adopt these principles.

II. GENERAL PRINCIPLES

1. The Declaration of Geneva of the WMA binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act in the patient's best interest when providing medical care."

2. It is the duty of the physician to promote and safeguard the health, well-being and rights of patients, including those who are involved in medical research. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.

3. Medical progress is based on research that ultimately must include studies involving human subjects.

4. The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best proven interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.

5. Medical research is subject to ethical standards that promote and ensure respect for all human subjects and protect their health and rights.

6. While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.

7. It is the duty of physicians who are involved in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects. The responsibility for the protection of research subjects must always rest with the physician or other health care professionals and never with the research subjects, even though they have given consent.

8. Physicians must consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and standards. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.

9. Medical research should be conducted in a manner that minimizes possible harm to the environment.

10. Medical research involving human subjects must be conducted only by individuals with the appropriate ethics and scientific education, training and qualifications. Research on patients or healthy volunteers requires the supervision of a competent and appropriately qualified physician or other health care professional.

11. Groups that are underrepresented in medical research should be provided appropriate access to participation in research.

12. Physicians who combine medical research with medical care should involve their patients in research only to the extent that this is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects.

13. Appropriate compensation and treatment for subjects who are harmed as a result of participating in research must be ensured.

III. RISKS, BURDENS AND BENEFITS

- In medical practice and in medical research, most interventions involve risks and burdens.

Medical research involving human subjects may only be conducted if the importance of the objective outweighs the risks and burdens to the research subjects.

- All medical research involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and groups involved in the research in comparison with foreseeable benefits to them and to other individuals or groups affected by the condition under investigation.

  Measures to minimize the risks must be implemented. The risks must be continuously monitored, assessed and documented by the researcher.

- Physicians may not be involved in a research study involving human subjects unless they are confident that the risks have been adequately assessed and can be satisfactorily managed.

  When the risks are found to outweigh the potential benefits or when there is conclusive proof of definitive outcomes, physicians must assess whether to continue, modify or immediately stop the study.

IV. VULNERABLE GROUPS AND INDIVIDUALS

- Some groups and individuals are particularly vulnerable and may have an increased likelihood of being wronged or of incurring additional harm.

  All vulnerable groups and individuals should receive specifically considered protection.

- Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research.

V. SCIENTIFIC REQUIREMENTS AND RESEARCH PROTOCOLS

- Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation. The welfare of animals used for research must be respected.

- The design and performance of each research study involving human subjects must be clearly described and justified in a research protocol.

  The protocol should contain a statement of the ethical considerations involved and should indicate how the principles in this Declaration have been addressed. The protocol should include information regarding funding, sponsors, institutional affiliations, potential conflicts of interest, incentives for subjects and information regarding provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study.

  In clinical trials, the protocol must also describe appropriate arrangements for post-trial provisions.

VI. RESEARCH ETHICS COMMITTEES

- The research protocol must be submitted for consideration, comment, guidance and approval to the concerned research ethics committee before the study begins. This committee must be transparent in its functioning, must be independent of the researcher, the sponsor and any other undue influence and must be duly qualified. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration.

  The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No amendment to the protocol may be made without consideration and approval by the committee. After the end of the study, the researchers must submit a final report to the committee containing a summary of the study's findings and conclusions.

VII. PRIVACY AND CONFIDENTIALITY

- Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information.

VIII. INFORMED CONSENT

- Participation by individuals capable of giving informed consent as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no individual capable of giving

informed consent may be enrolled in a research study unless he or she freely agrees.

- In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information.

  After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.

  All medical research subjects should be given the option of being informed about the general outcome and results of the study.

- When seeking informed consent for participation in a research study the physician must be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such situations the informed consent must be sought by an appropriately qualified individual who is completely independent of this relationship.

- For a potential research subject who is incapable of giving informed consent, the physician must seek informed consent from the legally authorized representative. These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the group represented by the potential subject, the research cannot instead be performed with persons capable of providing informed consent, and the research entails only minimal risk and minimal burden.

- When a potential research subject who is deemed incapable of giving informed consent is able to give assent to decisions about participation in research, the physician must seek that assent in addition to the consent of the legally authorized representative. The potential subject's dissent should be respected.

- Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or

mental condition that prevents giving informed consent is a necessary characteristic of the research group. In such circumstances the physician must seek informed consent from the legally authorized representative. If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee. Consent to remain in the research must be obtained as soon as possible from the subject or a legally authorized representative.

- The physician must fully inform the patient which aspects of their care are related to the research. The refusal of a patient to participate in a study or the patient's decision to withdraw from the study must never adversely affect the patient-physician relationship.

- For medical research using identifiable human material or data, such as research on material or data contained in biobanks or similar repositories, physicians must seek informed consent for its collection, storage and/or reuse. There may be exceptional situations where consent would be impossible or impracticable to obtain for such research. In such situations the research may be done only after consideration and approval of a research ethics committee.

IX. USE OF PLACEBO

- The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best proven intervention(s), except in the following circumstances:

  Where no proven intervention exists, the use of placebo, or no intervention, is acceptable; or

  Where for compelling and scientifically sound methodological reasons the use of any intervention less effective than the best proven one, the use of placebo, or no intervention is necessary to determine the efficacy or safety of an intervention

  and the patients who receive any intervention less effective than the best proven one, placebo, or no intervention will not be subject to additional risks of serious or irreversible harm as a result of not receiving the best proven intervention.

  Extreme care must be taken to avoid abuse of this option.

X. POST-TRIAL PROVISIONS

- In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial. This information must also be disclosed to participants during the informed consent process.

XI. RESEARCH REGISTRATION AND PUBLICATION AND DISSEMINATION OF RESULTS

- Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject.

- Researchers, authors, sponsors, editors and publishers all have ethical obligations with regard to the publication and dissemination of the results of research. Researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. All parties should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results must be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest must be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication.

XII. UNPROVEN INTERVENTIONS IN CLINICAL PRACTICE

In the treatment of an individual patient, where proven interventions do not exist, or other known interventions have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician's judgment it offers hope of saving life, re-establishing health or alleviating suffering. This intervention should subsequently be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information must be recorded and, where appropriate, made publicly available.